IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT

Inventor: Robert Kleiman

Docket No. FLORA.1100

Serial No. 09/899,432

Examiner: Shoba Kantamneni

Filing Date: 07/06/2001

Art Unit: 1617

Title: ANTIVIRAL COMPOSITION AND METHOD

RESPONSE TO NOTICE OF NON-COMPLIANT APPEAL BRIEF

MAIL STOP: APPEAL BRIEF - PATENTS
COMMISSIONER FOR PATENTS
P.O. BOX 1450
ALEXANDRIA, VIRGINIA 22313-1450

Dear Commissioner:

A brief, pursuant to 37 C.F.R. §41. 37, appealing the final decision of the Examiner dated 01/25/2008, wherein the Examiner finally rejected claims **91-102** of the present application, was originally submitted on 06/24/2008. A Notice of Non-Compliant Appeal Brief was subsequently mailed on 07/09/2008, indicating that the brief was not in compliance with 37 C.F.R. §41.37 because the brief did not contain the items required under 37 C.F.R. § 41.37 (c), and because the brief does not contain a statement of the status of all claims. This matter has now been corrected, and this paper is now submitted in response to the Notice of Non-Compliant Amendment

I. REAL PARTY IN INTEREST

The subject application is assigned to International Flora Technologies, Ltd. – the real party in interest. The assignment is recorded in the United States Patent and Trademark Office at Reel 013946, Frame 0576.

II. RELATED APPEALS AND INTERFERENCES

To Appellant's knowledge, there are no related appeals or interferences.

III. STATUS OF CLAIMS

1. All originally filed claims **1-90** have been cancelled or withdrawn. Specifically, claims **1,3-4,6-13, 15, 16, 18-19, 21- 22, 24-25, 27-28, 30- 31, 33- 34, 36-85, 87-88,** and **90** have been cancelled. Claims **2, 5, 14, 17, 20, 23, 26, 29, 32, 35, 86,** and **89** have been withdrawn. A copy of the claims being appealed, namely **91-102**, are provided in Appendix A. Claims **91-102** were previously presented.

2. Claims **91-92** are rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over U.S. Patent No. 5,952,392 to Katz *et al.* in view of PCT Publication No. WO 9602244 A1 to Sintov *et al.*, and further in view of PCT Publication No. WO 9920224 to Arquette *et al.*

3. Claims **93-102** are rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over U.S. Patent No. 5,952,392 to Katz *et al.* in view of PCT Publication No. WO 9602244 A1 to Sintov *et al.*, and further in view of U.S. Patent No. 4,874, 794 to Katz or U.S. Patent No. 5,070,107 to Katz.

IV. STATUS OF AMENDMENTS

On 11/05/2007, **claims 91, 93, 95, 97, 99** and **101** were amended in Appellant's Response to the non-final Office Action dated 05/03/2007. All amendments were entered by the Examiner, as acknowledged in the Final Office Action dated 01/25/2008. No subsequent amendments have been offered by Appellant.

V. SUMMARY OF CLAIMED SUBJECT MATTER

A representative embodiment of the present invention is directed to treatment of various viral infections and inflammatory diseases. [page 17, line 20; page 27, line 19] Suitable methods of treatment in accordance with the present invention include providing topical, intravenous, intramuscular, transdermal, trans-mucousal, and trans-membranal compositions. [page 7, lines 20-23; page 17, lines 9-19] Further representative embodiments of the present invention include use of long-chain monounsaturated alcohols in combination with salts of jojoba-derived fatty acids and mixed esters. [page 8, lines 1-4; page 9, lines 19-20; page 10, lines 6-24] These embodiments include:

91. A method for treating at least one of virus-induced and inflammatory diseases [page 17, line 20; page 27, line 19] said method comprising the step of providing a topical composition [page 17, lines 7-19] consisting essentially of:

at least one of octadecenol, eicosenol, docosenol, tetracosenol and hexacosenol [page 9, lines 10-18; page 13, lines 15-20] in a concentration of from 0.1 to 25 percent by weight of an admixed physiologically active carrier [page 16, line 20; page 17 line 2; page 22, lines 11-16];

at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH{=}CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion [page 12, line 11; page 13, line 16]; and

at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH{=}CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of

an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms ion [page 12, line 11; page 13, line 5].

92. The method of claim **91**, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight [page 12, lines 12-19].

93. A method for treating viral infections, said method comprising the step of intravenous delivery of a composition [page 18, lines 3-24] consisting essentially of:

an effective amount of from about 0.1 mg to about 2 gm per 50 kg of body weight of a compound comprising at least one C_{18} to C_{24} monounsaturated alcohol in a physiologically active carrier [page 18, lines 3-24];

at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion [page 12, line 11; page 13, line 16]; and

at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms [page 12, line 11; page 13, line 5].

94. The method of claim **93**, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight [page 12, lines 12-19].

95. A method for treating viral infections, said method comprising the step of intramuscular delivery of a composition [page 18, lines 3-24] consisting essentially of:

an effective amount of from about 0.1 mg to about 2 gm per 50 kg of body weight of a compound comprising at least one C_{18} to C_{24} monounsaturated alcohol in a physiologically active carrier [page 18, lines 3-24];

at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion [page 12, line 11; page 13, line 16]; and

at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms [page 12, line 11; page 13, line 5].

96. The method of claim **95**, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight [page 12, lines 12-19].

97. A method for treating viral infections, said method comprising the step of trans-mucousal delivery of a composition [page 19, lines 1-11] consisting essentially of:

an effective amount of from about 0.1 mg to about 2 gm per 50 kg of body weight of a compound comprising at least one C_{18} to C_{24} monounsaturated alcohol in a physiologically active carrier [page 18, lines 3-24];

at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion [page 12, line 11; page 13, line 16]; and

at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms [page 12, line 11; page 13, line 5].

98. The method of claim **97**, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight [page 12, lines 12-19].

99. A method for treating viral infections, said method comprising the step of transdermal delivery of a composition [page 17, lines 7-19] consisting essentially of:

an effective amount of from about 0.1 mg to about 2 gm per 50 kg of body weight of a compound comprising at least one C_{18} to C_{24} monounsaturated alcohol in a physiologically active carrier [page 18, lines 3-24];

at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion [page 12, line 11; page 13, line 16]; and

at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms [page 12, line 11; page 13, line 5].

100. The method of claim **99**, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight [page 12, lines 12-19].

101. A method for treating viral infections, said method comprising the step of trans-membranal delivery of a composition [page 17, lines 7-19] consisting essentially of:

an effective amount of from about 0.1 mg to about 2 gm per 50 kg of body weight of a compound comprising at least one monounsaturated alcohol having between 18 and 24 carbons [page 18, lines 3-24] in at least one of a physiologically acceptable liquid, cream,

gel and suppository carrier into at least one of an anus and vagina of an animal to be treated [page 17, lines 8-19];

at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion [page 12, line 11; page 13, line 16]; and

at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms [page 12, line 11; page 13, line 5].

102. The method of claim **101**, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight [page 12, lines 12-19].

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Issue 1:

Whether the references proposed by the Examiner effectively establishes a *prima facie* basis for obviousness under 35 U.S.C. § 103(a) for claims **91-92** and **93-102**; and more specifically, whether claims **91-92** are obvious over U.S. Patent No. 5,952,392 to Katz *et al.* in view of PCT Publication No. WO 9602244 A1 to Sintov *et al.*, and further in view of PCT Publication No. WO 9920224 to Arquette *et al.*; and whether claims **93-102** are obvious over U.S. Patent No. 5,952,392 to Katz *et al.* in view of PCT Publication No. WO 9602244 A1 to Sintov *et al.*, and further in view of U.S. Patent No. 4,874, 794 to Katz or U.S. Patent No. 5,070,107 to Katz.

VII. ARGUMENT

ISSUE 1: CLAIM REJECTIONS UNDER §103(a)

Claims **91-92** are rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over U.S. Patent No. 5,952,392 to Katz *et al.* in view of PCT Publication No. WO 9602244 A1 to Sintov *et al.*, and further in view of PCT Publication No. WO 9920224 to Arquette *et al.* Additionally, claims **93-102** are rejected under 35 U.S.C. §103 as purportedly being unpatentable over U.S. Patent No. 5,952,392 to Katz *et al.* in view of PCT Publication No. WO 9602244 A1 to Sintov *et al.*, and further in view of U.S. Patent No. 4,874, 794 to Katz or U.S. Patent No. 5,070,107 to Katz. Appellants respectfully traverse these rejections. Appellants further submit that a *prima facie* case of obviousness has not been established.

In light of the Supreme Court decision in *KSR v. Teleflex*, and the decisions by the Board of Patent Appeals and Interferences in *Ex Parte Smith*, *Ex Parte Kubin*, and *Ex Parte Catan*, any obviousness determination must be consistent with the traditional *Graham* factors. Thus, obviousness is determined according to (1) the scope and content of the prior art, (2) the level of ordinary skill in the art, (3) the differences between the prior art and the claimed invention, and (4) the extent of any objective indicia of nonobviousness.

Additionally, the Examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. In this case, the Examiner asserts that it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the Katz *et al.* reference, the Sintov *et al.* reference, the Arquette *et al.* reference, and the Katz references to arrive at the claimed invention. When asserting an obviousness rejection on these grounds, M.P.E.P. §4143 (G) requires the Examiner to "articulate the following:

(1) a finding that there was some teaching, suggestion, or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art to modify the reference to combine reference teachings;

(2) a finding that there was reasonable expectation of success; and

(3) whatever additional findings based on the *Graham* inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness."

With respect to the rejections of claims **91-92** and **93-102**, the Examiner has failed to assert a *prima facie* case of obviousness. As set forth *vide supra*, even if the Examiner had put forth a *prima facie* case, it is clear that the combination of the references, taken either alone or in conjunction with the knowledge of one of ordinary skill in the art, do not and cannot teach the claimed invention.

Claims 91-92

The Examiner proposes that Katz *et al.* (U.S. 5,952,392) "discloses that long chain fatty acids broadly including oleic acid (C18, one double bond, see col. 2 lines 12-15; col. 3, lines 5-8; col. 4, lines 26-28; col. 6, lines 28-35) or monounsaturated long chain alcohols broadly (*e.g.*, C18-C28, or octadecenol, docosenol, brassidyl alcohol) in their effective amounts with a physiologically compatible carrier (*e.g.*, cream or ointment applied to skin, or aqueous solution, *see* col. 12, EXAMPLE 5; Examples 12, 14-15; col.20, lines 34-35, and col. 22, lines 39-40 and 64) are useful in a pharmaceutical composition for topical application, intramuscular and intravenous injections, and methods of treating viral infections and virus-induced and inflammatory disease of skin and membranes because these compounds have antiviral activity *See* abstract; col. 1, lines 10-15 and 20-47; col. 3, lines 18-21; col.7, lines 62-67; col. 12, EXAMPLE 5; Examples 14-15 and col. 22-23." The Examiner further proposes that "compositions therein for use in treating viral infections comprise active ingredients [*sic*] or combination of compounds as the active ingredients selected from a group consisting of saturated aliphatic alcohols, mono-unsaturated aliphatic alcohols, mono-unsaturated aliphatic amides and aliphatic acids having a carbon chain length of 18-28 carbons, wherein the active ingredient is present in an amount of 0.1 to about 50% by weight of the final composition. *See* column 6, lines 28-36, lines 50-55. It is taught that the compositions therein are administered to the skin or a mucous membrane topically parenterally or by transmembranal penetration using a

cream, lotion, gel, ointment, suspension, aerosol spray or semi-solid formulation (*e.g.*, a suppository). *See* column 7, lines 62-67; column 24, claims 7-11."

However, Katz *et al.* (U.S. 5,952,392) does **not** disclose or teach use of "a method for treating at least one of virus-induced and inflammatory diseases [...] comprising the step of providing a topical composition consisting essentially of: at least one of octadecenol, eicosenol, docosenol, tetracosenol and hexacosenol in a concentration of from 0.1 to 25 percent by weight of an admixed physiologically active carrier; at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion; and at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms" as required by claim **91** of the present invention. Further, Katz *et al.* (U.S. 5,952,392) **does not teach or disclose use of *any* salts of fatty acids or mixed esters in a topical composition, let alone the salts of fatty acids and mixed esters of the instant invention *in combination with* monounsaturated long chain alcohols for treating virus-induced and inflammatory disease in accordance with the present invention**. In fact, the Examiner later admits as much by stating "[t]he prior art does not expressly disclose the employment of monounsaturated long chain alcohols in combination with the particular long chain fatty acids salts such as C20 acids, and fatty acid esters herein in a composition for treating virus-induced and inflammatory disease of skin and membranes". (emphasis in original).

In regard to Arquette *et al.* (WO 9920224), the Examiner proposes that Arquette *et al.* "discloses a pharmaceutical composition comprising the instant fatty alcohols at least 10% by weight (see particularly abstract and page 3 lines 15-22), and the instant fatty acid esters in their various percentages (see pages 4-8) with a physiologically compatible carrier for topical applications (see abstract and claims 1-12, especially claim 23). It is also taught that fatty acids such as oleic acid, myristic acid etc are used as emollients. *See* page 1, lines 24-29." However, Arquette *et al.* does not disclose "a method for treating at least one of virus-induced and inflammatory diseases [...] comprising the step of providing a topical composition consisting essentially of: at least one of octadecenol, eicosenol, docosenol, tetracosenol and hexacosenol in a concentration of from

0.1 to 25 percent by weight of an admixed physiologically active carrier; at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion; and at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms" as required by claim **91** of the present invention. In fact, Arquette *et al.* **does not teach or disclose use of *any* salts of fatty acids in a topical composition, let alone the salts of fatty acids of the instant invention *in combination with* monounsaturated long chain alcohols and mixed esters in accordance with Appellants' invention**.

Further, the Examiner proposes that "Sintov *et al.* discloses topical pharmaceutical compositions [*sic*] for the treatment of viral infections comprising salts of carboxylic acid such as alkali metal oleates, which include C18 salts. *See* abstract; page 2, bottom paragraph; page 3, lines 1-3, paragraph 5; page 7, EXAMPLE 1". However, Sintov *et al.* does not disclose "a method for treating at least one of virus-induced and inflammatory diseases [...] comprising the step of providing a topical composition consisting essentially of: at least one of octadecenol, eicosenol, docosenol, tetracosenol and hexacosenol in a concentration of from 0.1 to 25 percent by weight of an admixed physiologically active carrier; at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion; and at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms" as required by claim **91** of the present invention. In fact, the Sintov *et al.* reference explicitly teaches away from the use of other "any other antiviral agent" in combination with carboxylic acid salt in the treatment of viral diseases. *See* page 1, last paragraph. Sintov *et al.* **does not teach or disclose use of *any* long chain monounsaturated alcohols or mixed esters in a topical composition, let alone the monounsaturated long chain alcohols and mixed esters of the instant invention *in combination with* salts of fatty acids in accordance with the present invention.** Moreover, the Examiner admits as much in stating "[t]he prior art does not expressly disclose the employment of monounsaturated long chain alcohols in combination with long chain

fatty acids salts, and fatty acid esters herein in a composition for treating virus-induced and inflammatory disease of skin and membranes". (emphasis in original).

Further, as cited by Appellants in their response dated 11/05/2007, the salts of fatty acids in Sintov *et al.* are different from the salts of fatty acids as presented in claim **91**. Specifically, Sintov *et al.*; page 2 last paragraph, states "the present invention provides a topical pharmaceutical composition wherein said salt is selected from the group consisting of linoleates, elaidates, palitates, myristates, oleaates, malonates, succinates, adipates, pimelates, maleates, fumarates or azelates." None of these salts comprise "at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion."

Moreover, Sintov *et al.* teaches away from the salts in the present invention by stating that "[e]specially preferred for use in the present invention is a water-solubilized C_{16}-C_{18} carboxylic acid salt, such as akali oleate." The salts of the present invention comprise salts of long chain fatty acids that are carbon chain lengths of 20 or greater. It is well known that salts of long-chain fatty acids are less soluble in water as compared with shorter chain fatty acids salts, and therefore it would be unexpected that salts with chain lengths greater than 18 carbons would have similar and/or improved activity relative to the more-water-soluble materials, such as those materials suggested in Sintov *et al.* *See* 37 C.F.R. § 1.132 Affidavit of David Ashley, attached herewith as Exhibit 7.

In responses, in the Advisory Action dated 04/30/2008, the Examiner asserts that "the solubility of carboxylic acids in water alone with different chain lengths [*sic*] is not relevant. Note that the physiologically acceptable carrier in the instant claims can be water, alcohol etc. or mixtures of different solvents. The solubility of carboxylic acids with different chain lengths in alcohol/water mixtures will be different from solubility in water."

While accurately reciting a general rule that the solubility of carboxylic acids in alcohol/water mixtures is "different from the solubility in water", the Examiner fails to appreciate the crux of the issue. It is not the solubility of various different carboxylic acids (having different chain lengths) varies in different solvents that drives the distinction as between the salts disclosed in

Sintov *et al.* and the claimed invention. Rather, it is the fact that salts of longer chain fatty acids (greater than 18 carbons) are less soluble than salts of shorter-chain fatty acids. It follows that dramatic improved activity of the *less soluble* salts of longer-chain fatty acids in combination with the alcohols and mixed esters of the claimed invention is surprising, and could not have been expected based on the disclosure of Sintov *et al.*

In failing to appreciate this, the Examiner, in the Final Office Action, states:

> [i]t would have been obvious to one of ordinary skill in the art at the time of the invention to utilize the instant particular fatty acid salts such as C20 acid salts to treat viral infections in the methods of Katz et al. because Katz et al. (5,952,392) and Sintov et al teach the use of C18 acids and salts (sodium salt of oleic acid) in the method of treating viral infections....because of an expectation of success similar to that taught for structurally similar prior art species i.e. C18 acids, and salts, since structurally similar compounds usually have similar properties. See, e.g., Dillon 919, F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also Deuel, 51 F.3d at 1559, 25 USPQ2d at 1214, and if the claimed invention and the structurally similar prior art species share any useful property, that will generally be sufficient to motivate an artisan of ordinary skill to make the claimed species, In fact, similar properties may normally be presumed when compounds are very close in structure.

Appellants submit that the instant case is distinguishable from *In re Dillon* on several counts. First, the Examiner in *In re Dillon* proffered evidence of similarity between the prior art compound and the claimed compound in a composition. *Id* at 691. This reference showed that both the prior art compound and the claimed compound were structurally similar but also ***function*** similar. *Id.* ("[T]he Elliot reference shows equivalence between tetra-orthoesters [claimed compound] and tri-orthoesters [prior art compound] and that 'it is clear from the combined teachings of these references that the [claimed compound] would operate ... by the same mechanism."). In this case, the Examiner has provided no such evidence. Rather, the Examiner merely concludes that fatty acid salts in Sintov *et al.* and of the claimed invention are structurally similar, and that one would have been motivated to combine them with the other components of the claimed invention.

The Examiner has failed to appreciate Appellants' previous explanations of the narrow scope of Sintov *et al.* and that Sintov *et al.* explicitly taught away from combining salts of fatty acids with other compounds. Contrary to the Examiner's response to Appellants' assertions in regard to

Sintov *et al.*, the Sintov *et al.* reference cannot be used to "broadly teach[] that salts of carboxylic acids are employed in the compositions therein for treating viral infections" when Sintov *et al.* uses the limiting language of "consisting of" repeatedly to define the salts of fatty acids. *See, e.g.,* Sintov *et al*; page 2 and claim 2.

This lack of appreciation is exemplified in the Examiner's attempted use of *In re Haas* for the proposition that "the instant particular fatty acid salts are homologs, and thus they possess the same or substantially similar activities. Absent a showing of unexpected results, homologous compounds are considered to be obvious". The Examiner's application of *In re Haas* in this case is erroneous. The court in *In re Haas* determined homologs to be "adjacent compounds" that are technically novel, but where "there is no evidence that the claimed compounds behave differently from the known compounds or have any utility or properties which would be unobvious from knowledge of the utility and properties of the claimed (known) compounds." The Examiner makes the erroneous conclusion that salts of fatty acids of C20+ chain lengths are "homologs" of salts of fatty acids of shorter chain lengths. One of ordinary skill in the art recognizes that solubility decreases with increasing chain length, and with respect to salts of fatty acids as a delivery mechanism, the activity of shorter-chain fatty acid salts would be expected to be substantially different than that of the claimed longer-chain fatty acids salts. *See* Exhibit 7. Because the longer chain fatty acids of the claimed invention do not have solubility properties that map to those of shorter chain fatty acids in Sintov *et al.*, the fatty acid salts of the present invention cannot properly be viewed as homologs in accordance with *In re Haas.*

Indeed, the Examiner has not addressed the knowledge of one of ordinary skill in the art that long-chain fatty acid salts are generally less soluble than shorter-chain fatty acids, and therefore it would not have been expected that long-chain fatty acid salts would provide the proven antiviral activity of the claimed invention. Specifically, "a 100-fold increase in antiviral activity is observed where the expectation would be that the delivery mechanism would not traffic the antiviral as effectively due to the decreased solubility associated with fatty acid salts having chain lengths of 20 carbons or greater." *See* Exhibit 7.

Appellants respectfully request that judicial notice be taken that the Examiner has been either unwilling or unable to proffer any reference or teaching in the art that speaks to the effectiveness of ***long chain fatty acid salts alone or in combination with the fatty acid esters and long chain alcohols of the claimed invention*** *for the purpose of treating viral inventions. Instead, the Examiner asserts factually unsupported conclusions that salts of shorter-chain fatty acids (such as those in Sintov et al.) may be modified to become long chain fatty acid salts* ***and*** *combined with fatty acid esters and long chain alcohols. As such, Appellants respectfully submit that the Examiner has failed to provide a prima facie case of obviousness, and that the instant §103 rejection is improper and must be withdrawn.*

That notwithstanding, even if the Examiner had properly asserted a *prima facie* case of obviousness, Appellants have provided ample evidence of unexpected, surprising results to rebut any such assumption. *See* application as filed, pages 23-26, and the 37 C.F.R. §1.132 affidavits of David Ashley and Robert Kleiman previously submitted on 11/15/2007, attached as Exhibits 5-6.

Next the Examiner proposes that "[o]ne of ordinary skill in the art at the time the invention was made would have been motivated to employ the instant long chain fatty acid salt in combination with long chain alcohols because 1) the instant long chain fatty acid salts is a homolog of alkali metal oleate, and will possess similar anti-viral properties as that of the alkali metal oleate and 2) monounsaturated long chain alcohols are known to be useful to treat virus-induced and inflammatory disease of skin and membranes according to Katz et al (5,952,392) and Sintov et al." and that there was a "reasonable expectation [sic] of success of obtaining a pharmaceutical composition for treating virus-induced and inflammatory disease of skin and membranes."

Appellants respectfully submit that the Examiner's assertion is *non sequitur* in view of claim **91**, to the extent that salts of fatty acids of the present invention cannot properly be characterized as a "homolog of alkali metal oleate"; and moreover, the combination of salts with monounsaturated alcohols and mixed fatty acid esters is not taught in the references provided by the Examiner, nor does the Examiner provide reference to knowledge generally available in the art. Furthermore, the combination of the present invention for the purpose of treatment of viral

and inflammatory diseases is also not taught or suggested in the references provided by the Examiner, or in the knowledge generally available in the art.

The Examiner proposes that:

> [o]ne of ordinary skill in the art would have reasonably expected that combining the instant fatty acid esters taught by Arquette *et al.* with the monounsaturated fatty alcohols, and the salts of fatty acids [*sic*] in a pharmaceutical composition would improve the therapeutic effect for treating virus-induced and inflammatory disease of skin and membranes because 1) fatty acid esters are known to be used as an emollient [*sic*] in pharmaceutical composition comprising monounsaturated long chain alcohols, and 2) further according to Arquette emollients have beneficial effects such as softening, smoothening skin, reduce skin roughness, cracking and irritation of skin. Thus, one of ordinary skill in the art would have reasonably expected that the combination of the instant fatty acid esters taught by Arquette *et al.* with the instant fatty alcohols, and the salts of oleic acid *i.e.*, instant salts of fatty acids in a pharmaceutical composition would have at least additive therapeutic effects and also provide additional benefits such as softening, smoothening of skin."

The combination of fatty acid esters of Arquette *et al.*, fatty alcohols and salts of oleic acid to provide therapeutic effects does not teach or suggest, taken alone or in combination with the other cited references, the present invention. Specifically, "a method for treating at least one of virus-induced and inflammatory diseases [...] comprising the step of providing a topical composition consisting essentially of: at least one of octadecenol, eicosenol, docosenol, tetracosenol and hexacosenol in a concentration of from 0.1 to 25 percent by weight of an admixed physiologically active carrier; at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH{=}CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion; and at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH{=}CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms", as required by claim **91**.

Moreover, the suggested combination that the Examiner proposes does not appreciate the surprising, synergistic effects of the combination of the present invention. *See* Exhibits 5 and 6 (discussing the 100-fold increase in antiviral activity of the present invention as compared to the antiviral activity of the alcohol alone).

Notwithstanding that these affidavits clearly state that "K100 refers to the combination of monounsaturated long chain alcohols, jojoba-derived fatty acid salts, and fatty acid esters (specifically, jojoba esters)", the Examiner states that "the declaration does not provide any information with respect to which unsaturated long chain alcohol, fatty acid salt, and ester are employed in the combination K100."

In the Advisory Action, the Examiner responded, expressing concern that "there is no data provided for the individual fatty acid salts, and esters" and that the "declaration merely provides antiviral activity data for n-docosanol alone, and does not provide antiviral activity data for the individual fatty acid salts and esters. Accordingly, the data is not convincing with respect to the synergistic effects of the combination of the present invention."

However, the Examiner has not rebutted the various references made in the application as filed to the "composition of the present invention", which clearly refers to three components: alcohols, wax esters, and salts of fatty acids. *See* application as filed, page 13, lines 1-13. For example; page 11, lines 23-26 of the application clearly refer to the testing of "the composition of the present invention". Page 10, lines 3 and page 12, line 22 of the application as filed clearly indicate that components of "the present invention" include "unsaturated wax esters" and hydrolyzed wax esters and "monounsaturated long chain alcohols and salts of long chain fatty acids." Appellants respectfully submit that data relating to concentrations of K100 were provided in Exhibit 1 of Exhibits 5 and 6, which is derived from pages 26-27 of the application as filed.

In summary, where the Examiner does not provide any teaching or reference for the claimed combination, nor an explanation as to how the unexpected, synergistic results of the claimed combination could be predictable, an obviousness rejection cannot be proper. Therefore, Appellants respectfully request that the rejections of claims **91-92** under §103 be withdrawn.

Claims 93-102

*Appellants hereby incorporate and reiterate all arguments/remarks made under the previous section relating to the rejection of claims **91-92** under §103 in this section.*

The Examiner asserts the following:

> "Katz *et al.* (5,952,392) does not explicitly teach the effective amount of the monounsaturated alcohol as from about 0.1 mg to about 2gm per 50 kg of body weight.
>
> Katz *et al.* (4,874,794) discloses that the effective amounts of long chain fatty alcohols broadly (*e.g.*, C20-C26) with a physiologically compatible carrier in a pharmaceutical composition for topical application for methods of treating viral infections and skin inflammations are 0.1 to 25 percent by weight. See abstract; col.3, lines 63-8, claims 1-2.
>
> Katz *et al.* (5,070,107) discloses that the effective amounts of long chain fatty alcohols broadly (*e.g.*, C27-C32) with a physiologically compatible carrier in a pharmaceutical composition for topical application and intramuscular intravenous injections for methods of treating viral infections and skin inflammations are 0.1 mg to 2 g/per 50kg of body weight. See abstract, co.3 lines 63-68, claims 1-2.
>
> One of ordinary skill in the art would have been motivated to optimize the effective amounts of instantly claimed long chain monounsaturated alcohols in the composition because Katz *et al.* '794, and '107 teaches effective amounts of structurally similar long chain fatty alcohols active agents for treating viral infections and skin inflammations as 0.1 mg to 2 g/per 50 kg of body weight. Further, it has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients in a composition in order to achieve a beneficial effect. *See In re Boesch,* 205 USPQ 215 (CCPA 1980)."

Appellants respectfully submit that optimization of the teachings of the Katz *et al.* ('392, '794, '107) references would not result in the combination of Appellants' invention. As discussed at length above, the combination of the present invention could not have been deduced from the prior art, nor was the nature of the synergistic effect of the combination of the present invention known or appreciated in the prior art. *See* Exhibits 5 and 6. Specifically, data presented in Exhibits 5 and 6 show an at least 100-fold increase in antiviral effectiveness against the HSV-1 strain (6343). *Even if* the components of the combination of the present invention were taught separately, the resulting combination could not have been characterized as merely an optimization of parameters to obtain a "beneficial effect" in accordance with *In re Boesch.*

Appellants respectfully request judicial notice be taken that the Examiner has been either unwilling or unable to provide any combination of references or knowledge generally available in the art to teach the claimed combination and/or provide support for the Examiner's assertion that the claimed combination merely optimizes parameters to obtain a "beneficial effect" in accordance with In re Boesch.

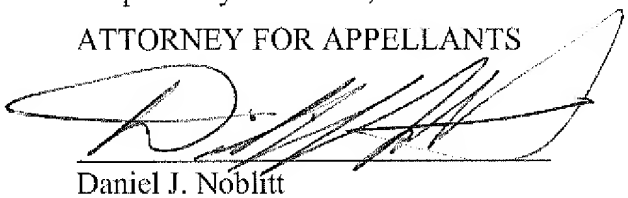
Accordingly, the Examiner's proposition that an optimization of parameters of compositions taught in the prior art could account for the 100-fold increase in antiviral activity seen as a result of the combination of the present invention fails on two counts: (1) the prior art does not teach the composition of the present invention (*see discussion above*), and (2) the resulting effect of the combination of the present invention is more than beneficial, rather it may be more aptly characterized as synergistic and surprising (*i.e.*, substantially greater than the sum of the individual component parts). *See* Exhibit 7.

As in the instant case, where the Examiner has not provided any teaching or reference for the claimed combination, nor any explanation as to how the unexpected, synergistic results of the claimed combination could be predicted, an obviousness rejection may not be properly applied. Therefore, Appellants respectfully request that the rejections of claims **93-102** under §103 be withdrawn.

CONCLUSION

Appellants therefore respectfully request reversal of the final rejection and the allowance of the subject application.

Respectfully submitted,
ATTORNEY FOR APPELLANTS



Date: JULY 18, 2008

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APPENDIX A (CLAIMS APPENDIX)

91. A method for treating at least one of virus-induced and inflammatory diseases, said method comprising the step of providing a topical composition consisting essentially of:

at least one of octadecenol, eicosenol, docosenol, tetracosenol and hexacosenol in a concentration of from 0.1 to 25 percent by weight of an admixed physiologically active carrier;

at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion; and

at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms.

92. The method of claim **91**, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight.

93. A method for treating viral infections, said method comprising the step of intravenous delivery of a composition consisting essentially of:

an effective amount of from about 0.1 mg to about 2 gm per 50 kg of body weight of a compound comprising at least one C_{18} to C_{24} monounsaturated alcohol in a physiologically active carrier;

at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion; and

at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms.

94. The method of claim **93**, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight.

95. A method for treating viral infections, said method comprising the step of intramuscular delivery of a composition consisting essentially of:

an effective amount of from about 0.1 mg to about 2 gm per 50 kg of body weight of a compound comprising at least one C_{18} to C_{24} monounsaturated alcohol in a physiologically active carrier;

at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion; and

at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms.

96. The method of claim **95**, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight.

97. A method for treating viral infections, said method comprising the step of trans-mucousal delivery of a composition consisting essentially of:

an effective amount of from about 0.1 mg to about 2 gm per 50 kg of body weight of a compound comprising at least one C_{18} to C_{24} monounsaturated alcohol in a physiologically active carrier;

at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion; and

at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms.

98. The method of claim **97**, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight.

99. A method for treating viral infections, said method comprising the step of transdermal delivery of a composition consisting essentially of:

an effective amount of from about 0.1 mg to about 2 gm per 50 kg of body weight of a compound comprising at least one C_{18} to C_{24} monounsaturated alcohol in a physiologically active carrier;

at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion; and

at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms.

100. The method of claim **99**, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight.

101. A method for treating viral infections, said method comprising the step of trans-membranal delivery of a composition consisting essentially of:

an effective amount of from about 0.1 mg to about 2 gm per 50 kg of body weight of a compound comprising at least one monounsaturated alcohol having between 18 and 24 carbons in at least one of a physiologically acceptable liquid, cream, gel and suppository carrier into at least one of an anus and vagina of an animal to be treated;

at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion; and

at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms.

102. The method of claim **101**, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight.

APPENDIX B (EVIDENCE APPENDIX)

(1) Appellants' 37 C.F.R. §1.132 affidavit of Robert Kleiman, submitted 04/26/2006, entered in the record by the Examiner in the Non-Final Office Action dated 05/11/2007, and attached hereto as Exhibit 1.

(2) Appellants' 37 C.F.R. §1.132 affidavit of David Ashley, submitted 04/26/2006, entered in the record by the Examiner in the Non-Final Office Action dated 05/11/2007, and attached hereto as Exhibit 2.

(3) Appellants' 37 C.F.R. §1.132 affidavit of Robert Kleiman, submitted 11/15/2007, entered into the record by the Examiner in the Final Office Action dated 01/25/2008, and attached hereto as Exhibit 3.

(4) Appellants' 37 C.F.R. §1.132 affidavit of David Ashley, submitted 11/15/2007, entered into the record by the Examiner in the Final Office Action dated 01/25/2008, and attached hereto as Exhibit 4.

(5) Appellants' 37 C.F.R. §1.132 affidavit of Robert Kleiman, submitted 11/15/2007, entered into the record by the Examiner in the Final Office Action dated 01/25/2008, and attached hereto as Exhibit 5.

(6) Appellants' 37 C.F.R. §1.132 affidavit of David Ashley, submitted 11/15/2007, entered into the record by the Examiner in the Final Office Action dated 01/25/2008, and attached hereto as Exhibit 6.

(7) Appellants' 37 C.F.R. §1.132 affidavit of David Ashley, submitted 03/25/2008, entered into the record by the Examiner in the Advisory Action dated 04/30/2008, and attached hereto as Exhibit 7.

APPENDIX C (RELATED PROCEEDINGS APPENDIX)

None

Exhibit 1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Kleiman *et al.*	Atty Docket No.:	FLORA.1100
Serial No.:	09/899,432	Group Art Unit:	1617
Filed:	07/06/2001	Examiner:	Shobha Kantamneni

TITLE: **ANTIVIRAL COMPOSITION AND TREATMENT METHOD**

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class mail in an envelope addressed to "Mail Stop: Amendment Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" on.

Date: _____ By: _____

Printed Name: _____

AFFIDAVIT
PURSUANT TO 37 C.F.R. §1.132

Assistant Commissioner of Patents
Alexandria, VA 22313-1450

Dear Assistant Commissioner:

STATE OF ARIZONA)
:
COUNTY OF MARICOPA)

I, Robert Kleiman, being duly sworn, depose and say as follows:

I have been employed by International Flora Technologies, Inc., since 1995 where I serve as Technical Services Manager. I have over 40 years of research experience involving industrial oils and cosmetic formulations. Previously, I was employed at the National Center for Agricultural Utilization Research, where I served as Research Leader for the New Crops Group. During my tenure at NCAUR, I investigated the chemistry of new industrial oil seed crops. This research directly resulted in over 150 publications and patents. I have been invited to give presentations regarding this work both domestically and internationally.

In 1993, I was awarded the Outstanding Researcher Award by the Association for the Advancement of Industrial Crops (AAIC). In 2002, I received the AAIC's highest award - Anson Ellis Thompson Career Service Award. I am a member of the American Oil Chemists' Society and the Association for the Advancement of Industrial Crops.

I have undertaken an extensive review of United States Patent Application Serial No. 09/899,432. The invention referenced therein is directed to methods for treating virus-induced and inflammatory diseases utilizing topical compositions that include monounsaturated long chain alcohols in combination with long chain fatty acid salts and fatty acid esters. This combination accounts for a dramatic increase in antiviral activity, as shown in Tables 2 and 3 of the application as filed. Specifically, Tables 2 and 3 show the relative plaque growth 48 hours after the introduction of this combination (in various concentrations) into wells containing a standard HSV-1 control (strain 6143) (see Table 2) and the acyclovir resistant HSV-1 (strain 15671) (see Table 3). What is surprising is that this combination was effective against the treatment resistant strain, and that it required lower IC_{50} concentrations than the non-resistant strain. Moreover, the combination demonstrated no cytotoxicity up to, and including, concentrations of 250 mg/ml, the highest concentration tested.

Further, the cellular proliferation of cells exposed to the Herpes Simplex Type 1 Virus treated with the present invention showed up to a 238% increase over untreated (or control) cells in a microculture tetrazolium assay, as shown in Table 1 of the application as filed. Thus, the combination of monounsaturated long chain alcohols with long chain fatty acid salts and fatty acid esters creates unexpected cytotoxicity profiles.

The cytotoxicity profiles of long chain alcohols, salts of fatty acids, and mixed fatty acid esters alone is different from that of the combination. While it is known that long chain alcohols and fatty acid esters alone may increase antiviral activity, what is not known and could not have been predicted is the combination of long chain alcohols, salts of fatty acids and mixed esters would dramatically increase antiviral activity. Upon reviewing United States Patent Application Serial No. 09/899,432, based on the totality of my skill and experience, I am surprised and would not have expected the significant increase in

antiviral activity of the combination of long chain alcohols, salts of fatty acids and mixed esters as disclosed in United States Patent Application Serial No. 09/899,432.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true. I further declare that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful and false statements may jeopardize the validity of the subject patent application or any patent issued thereon.

I further declare that I have received no special compensation or consideration for making this affidavit, nor have I been in any way told, either directly or by implication or inference, by anyone that my employment by International Flora Technologies, Inc., or my professional advancement or other matters of personal or professional interest to me depend in any way on whether or not I make this affidavit or the content thereof. I further declare that I make this affidavit of my own free will and choice without any duress or influence of any kind, believing fully in the truth of the statements made by myself herein.

Robert Kleiman

I, Carol Hynes, a Notary Public in and for the County and State aforesaid, do hereby certify that Robert Kleiman, whose name is subscribed to the foregoing instrument, appeared before me this day in person and acknowledge that he signed, sealed and delivered the said instrument as his free and voluntary act and deed for the uses and purposes therein set forth.

Given under my hand and Notary Seal this 17th day of April 2007.

My commission expires on Nov. 29, 2007

SEAL

OFFICIAL SEAL
CAROL HYNES
NOTARY PUBLIC - State of Arizona
MARICOPA COUNTY
My Comm. Expires Nov. 29, 2007

Exhibit 2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Kleiman *et al.*	Atty Docket No.:	FLORA.1100
Serial No.:	09/899,432	Group Art Unit:	1617
Filed:	07/06/2001	Examiner:	Shobha Kantamneni

TITLE: **ANTIVIRAL COMPOSITION AND TREATMENT METHOD**

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class mail in an envelope addressed to "Mail Stop: Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" on

Date: _____ By: _____

Printed Name: _____

AFFIDAVIT
PURSUANT TO 37 C.F.R. §1.132

Assistant Commissioner of Patents
Alexandria, VA 22313-1450

Dear Assistant Commissioner:

STATE OF ARIZONA)
:
COUNTY OF MARICOPA)

I, David Ashley, being duly sworn, depose and say as follows:

I received a Bachelors of Science in Chemistry from Arizona State University in May of 1987. I have been employed by International Flora Technologies, Inc., (Technical Department) since 2003 where I serve as a chemist. Previously, I was employed at Safety-Kleen Systems, Inc., where I served as Compliance Manager from 2002-2003. I have also worked in various technical and managerial capacities at Onyx Environmental Services (Saleseo Systems USA, Inc.), ADFlex Solutions Inc., and Revlon Consumer Products Corporation. I have over fourteen years of experience in analytical chemistry, environmental, health, and safety management. I am a Certified Hazardous Material Manager, and a member of the American Chemical Society.

I have undertaken an extensive review of United States Patent Application Serial No. 09/899,432. The invention referenced therein is directed to methods for treating virus-induced and inflammatory diseases utilizing topical compositions that include monounsaturated long chain alcohols in combination with long chain fatty acid salts and fatty acid esters. This combination results in a dramatic increase in antiviral activity, as shown in Tables 2 and 3 of the application as filed. Specifically, Tables 2 and 3 show the relative plaque growth 48 hours after the introduction of this combination (in various concentrations) into wells containing a standard HSV-1 control (strain 6143) (see Table 2) and the acyclovir resistant HSV-1 (strain 15671) (see Table 3). What is surprising is that this combination was effective against the treatment resistant strain, and that it required lower IC_{50} concentrations than the non-resistant strain. Moreover, the combination demonstrated no cytotoxicity up to, and including, concentrations of 250 mg/ml, the highest concentration tested.

Further, the cellular proliferation of cells exposed to the Herpes Simplex Type 1 Virus treated with the present invention showed up to a 238% increase over untreated (or control) cells in a microculture tetrazolium assay, as shown in Table 1 of the application as filed. Thus, the combination of monounsaturated long chain alcohols with long chain fatty acid salts and fatty acid esters creates unexpected cytotoxicity profiles.

The cytotoxicity profiles of long chain alcohols, salts of fatty acids, and mixed fatty acid esters alone is different from that of the combination. While it is known that long chain alcohols and fatty acid esters alone may increase antiviral activity, what is not known and could not have been predicted is the combination of long chain alcohols, salts of fatty acids and mixed esters would dramatically increase antiviral activity. Upon reviewing United States Patent Application Serial No. 09/899,432, based on the totality of my skill and experience, I am surprised and would not have expected the significant increase in antiviral activity of the combination of long chain alcohols, salts

of fatty acids and mixed esters as disclosed in United States Patent Application Serial No. 09/899,432.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true. I further declare that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful and false statements may jeopardize the validity of the subject patent application or any patent issued thereon.

I further declare that I have received no special compensation or consideration for making this affidavit, nor have I been in any way told, either directly or by implication or inference, by anyone that my employment by International Flora Technologies, Inc., or my professional advancement or other matters of personal or professional interest to me depend in any way on whether or not I make this affidavit or the content thereof. I further declare that I make this affidavit of my own free will and choice without any duress or influence of any kind, believing fully in the truth of the statements made by myself herein.

David Ashley

I, Carol Hynes, a Notary Public in and for the County and State aforesaid, do hereby certify that David Ashley, whose name is subscribed to the foregoing instrument, appeared before me this day in person and acknowledge that he signed, sealed and delivered the said instrument as his free and voluntary act and deed for the uses and purposes therein set forth.

Given under my hand and Notary Seal this 14th day of April 2006.

My commission expires on Nov. 29, 2007

SEAL

OFFICIAL SEAL
CAROL HYNES
NOTARY PUBLIC - State of Arizona
MARICOPA COUNTY
My Comm. Expires Nov. 29, 2007

Exhibit 3

FLORA.1100

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Kleiman *et al.*	Atty Docket No.:	FLORA.1100
Serial No.:	09/899,432	Group Art Unit:	1617
Filed:	07/06/2001	Examiner:	Shobha Kantamneni

TITLE: **ANTIVIRAL COMPOSITION AND TREATMENT METHOD**

CERTIFICATE OF MAILING

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Date: _____ By: _____

Printed Name: _____

AFFIDAVIT
PURSUANT TO 37 C.F.R. §1.132

Assistant Commissioner of Patents
Alexandria, VA 22313-1450

Dear Assistant Commissioner:

STATE OF ARIZONA)
:
COUNTY OF MARICOPA)

I, Robert Kleiman, being duly sworn, depose and say as follows:

I have been employed by International Flora Technologies, Inc., since 1995 where I serve as Senior Chemist. I have over 40 years of research experience involving industrial oils and cosmetic formulations. Previously, I was employed at the National Center for Agricultural Utilization Research ("NCAUR"), where I served as Research Leader for the New Crops Group. During my tenure at NCAUR, I investigated the chemistry of new industrial oil seed crops. This research directly resulted in over 150 publications and patents. I have been invited to give presentations regarding this work both domestically and internationally.

In 1993, I was awarded the Outstanding Researcher Award by the Association for the Advancement of Industrial Crops (AAIC). In 2002, I received the AAIC's highest award - Anson Ellis Thompson Career Service Award. I am a member of the American Oil Chemists' Society and the Association for the Advancement of Industrial Crops.

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A logarithmic regression to find the 50% kill concentration was performed on the results of the combination of the present invention and on the results of n-docosanol alone. When comparing the kill concentrations of

the combination of the present invention and n-docosanol alone, it is shown that the combination of the present invention is approximately 100 times more effective than n-docosanol alone in killing the HSV-1 Strain 6143.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true. I further declare that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful and false statements may jeopardize the validity of the subject patent application or any patent issued thereon.

I further declare that I have received no special compensation or consideration for making this affidavit, nor have I been in any way told, either directly or by implication or inference, by anyone that my employment by International Flora Technologies, Inc., or my professional advancement or other matters of personal or professional interest to me depend in any way on whether or not I make this affidavit or the content thereof. I further declare that I make this affidavit of my own free will and choice without any duress or influence of any kind, believing fully in the truth of the statements made by myself herein.

Robert Kleiman

I, Carol Hynes, a Notary Public in and for the County and State aforesaid, do hereby certify that Robert Kleiman, whose name is subscribed to the foregoing instrument, appeared before me this day in person and acknowledge that he signed, sealed and delivered the said instrument as his free and voluntary act and deed for the uses and purposes therein set forth.

Given under my hand and Notary Seal this 7th day of Nov 2007.

My commission expires on Nov. 29, 2007

SEAL

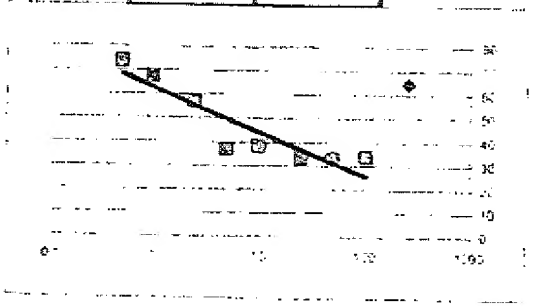
OFFICIAL SEAL
CAROL HYNES
NOTARY PUBLIC - State of Arizona
MARICOPA COUNTY
My Comm. Expires Nov. 29, 2007

EXHIBIT 1

A

n-Docosanol

Conc (mg/mL)	% Compared to Untreated Colonies
250	64.58
100	34.03
50	33.33
25	33.33
10	38.19
5	36.81
2.5	56.94
1	67.36
0.5	73.61



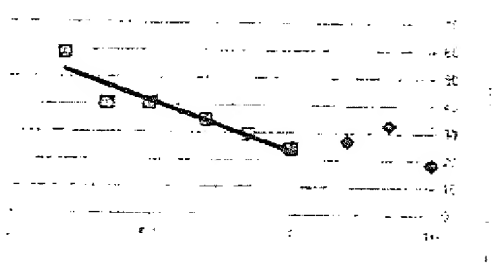
y = -8.0685643947301Ln(x) + 62.7072648371868

x= 4.830257
y= 50.00008

B

K-100

Conc (mg/mL)	% Compared to Untreated Colonies
10	18.3
5	32.7
2.5	26.8
1	24.2
0.5	29.4
0.25	34.6
0.1	40.5
0.05	40.5
0.025	58.7



y = -8.01198033621572Ln(x) + 23.2057165088178

x= 0.035286
y= 50.00003

result **136.8904305**

100 times more effective

EXHIBIT 1

Exhibit 4

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Kleiman *et al.*	Atty Docket No.:	FLORA.1100
Serial No.:	09/899,432	Group Art Unit:	1617
Filed:	07/06/2001	Examiner:	Shobha Kantamneni

TITLE: **ANTIVIRAL COMPOSITION AND TREATMENT METHOD**

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class mail in an envelope addressed to " Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" on:

Date: _____ By: _____

Printed Name: _____

AFFIDAVIT
PURSUANT TO 37 C.F.R. §1.132

Assistant Commissioner of Patents
Alexandria, VA 22313-1450

Dear Assistant Commissioner:

STATE OF ARIZONA)
:
COUNTY OF MARICOPA)

I, David Ashley, being duly sworn, depose and say as follows:

I received a Bachelors of Science in Chemistry from Arizona State University in May of 1987. I have been employed by International Flora Technologies, Inc., (Technical Department) since 2003 where I serve as a chemist. Previously, I was employed at Safety-Kleen Systems, Inc., where I served as Compliance Manager from 2002-2003. I have also worked in various technical and managerial capacities at Onyx Environmental Services (Salesco Systems USA, Inc.), ADFlex Solutions Inc., and Revlon Consumer Products Corporation. I have over fourteen years of experience in analytical chemistry, environmental, health, and safety management. I am a Certified Hazardous Material Manager, and a member of the American Chemical Society.

I have undertaken an extensive review of United States Patent Application Serial No. 09/899,432. The invention referenced therein is directed to methods for treating virus-induced and inflammatory diseases utilizing compositions that include monounsaturated long chain alcohols in combination with long chain fatty acid salts and fatty acid esters. This combination accounts for a dramatic increase in antiviral activity including against the Herpes Simplex Virus (HSV-1) strain (6143), as discussed on pages 26-27 of the application as filed.

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David Ashley

I, Carol Hynes, a Notary Public in and for the County and State aforesaid, do hereby certify that David Ashley, whose name is subscribed to the foregoing instrument, appeared before me this day in person and acknowledge that he signed, sealed and delivered the said instrument as his free and voluntary act and deed for the uses and purposes therein set forth.

Given under my hand and Notary Seal this 7th day of Nov 2007.

My commission expires on Nov 29, 2007

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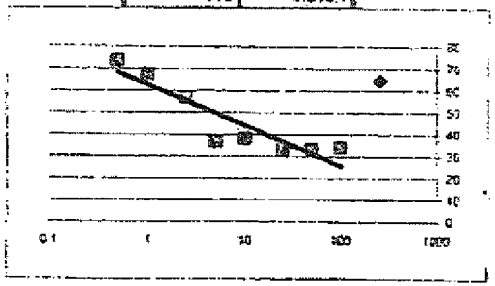

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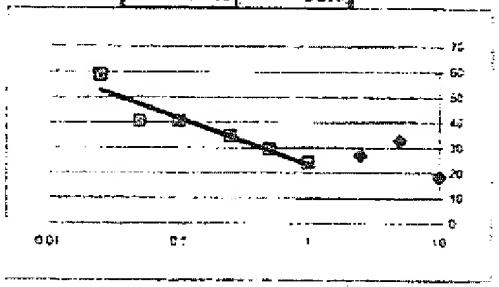

y = -8.011980336215 72Ln(x) + 23.2057185088178

x= 0.035286
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result 136.8904305
100 times more effective

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Serial No.:	09/899,432	Group Art Unit:	1617
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TITLE: **ANTIVIRAL COMPOSITION AND TREATMENT METHOD**

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Date: _____ By: _____

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PURSUANT TO 37 C.F.R. §1.132

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Alexandria, VA 22313-1450

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:
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It is known that the fatty acids of jojoba are made of essentially all cis-isomers. *See* excerpt from "Jojoba: New Crops for Arid Lands, New Raw Material for Industry", Report of an Ad Hoc Panel of the Advisory Committee on Technology Innovation Board on Science and Technology for International Development Office of International Affairs National Research Council (1985), *attached as* Exhibit 1. This is evidenced by, for example, the fact that no trans-isomers are present prior to isomerization of jojoba oil. *See* Jaime Wisniak, THE CHEMISTRY AND TECHNOLOGY OF JOJOBA OIL, p. 87 (1987), *attached as* Exhibit 2. In other words, jojoba oil that has not undergone the process of isomerization is considered "trans-free".

Additionally, when fatty alcohols and fatty acids derived from jojoba oil are analyzed using infrared spectrophotometry, an absence of absorption at 10.36 microns indicates that all ethylenic bonds [of fatty alcohols and fatty acids derived from jojoba oil] are *cis* in geometric configuration. *See* Wisniak, at p. 43, *attached as* Exhibit 3. Therefore, fatty acids and fatty alcohols derived from jojoba oil are considered "trans-free".

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true. I further declare that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or

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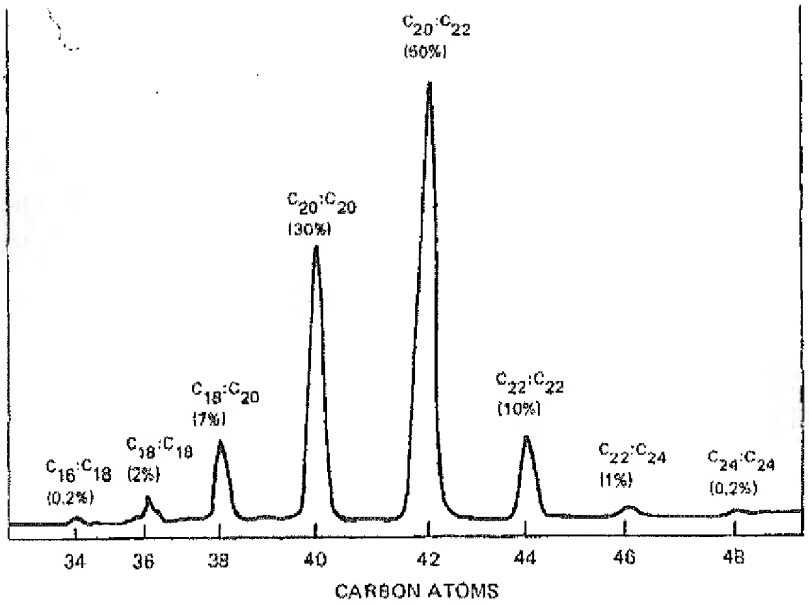
EXHIBIT 1



Jojoba oil esters are made up of fatty alcohols and fatty acids that are predominantly 20 or 22 carbon atoms long. Compared with most vegetable oils, the carbon chain lengths are remarkably uniform. (Information from T.K. Miwa)

alcohols are a mixture of eicosanol and docosanol, with smaller quantities of hexacosanol and alcohols of lower molecular weight.

The acids and alcohols that make up jojoba oil each have a single double bond. Moreover, all double bonds are in the ω_9 position (i.e., between carbon 9 and carbon 10, counting from the methyl end). This is a remarkable molecular purity, and the double bond position is different from that usually found in vegetable oils.

The nature of the oil can be grossly changed by reactions at the double bonds and ester functions, and many new products can result. One research laboratory in Israel, for example, has produced more than 40 different jojoba-based chemicals that appear to have commercial industrial applications.*

As in other natural oils, the double bonds in fresh jojoba oil are all in the *cis* configuration. However, they can be easily isomerized (twisted around in space), using as catalysts traces of selenium, nitrogen oxides, or active earth. This produces an equilibrium mixture with 20 percent *cis* and 80 percent *trans* double bonds. This simple process dramatically transforms the liquid into a soft, opaque cream resembling face cream. It can be stopped at various intermediate degrees of

* Information from A. Shani and J. Wisniak.

JOJOBA

New Crop for Arid Lands, New Raw Material for Industry

Report of an Ad Hoc Panel of the
Advisory Committee on Technology Innovation
Board on Science and Technology
for International Development
Office of International Affairs
National Research Council

NATIONAL ACADEMY PRESS
Washington, D.C. 1985

EXHIBIT 2

THE CHEMISTRY AND TECHNOLOGY OF

JOJOBA OIL

JAIME WISNIAK

American Oil Chemists' Society
Champaign, Illinois

percent nitrous acid. A 70% yield of *trans* isomer was obtained with no migration of the double bond. Their results indicated that the isomerization is induced initially by the nitrogen dioxide anion and followed immediately by complex formation between the excited triplet anion and the olefin. Crystallization of the final product yielded a solid that contained 96–97% of the *trans* form (brassidic acid) and melted at 58–59 C. The *cis* and *trans* double bonds in erucic and brassidic acids were identified by NMR, and absence of double bond migration was verified by reductive microozonolysis-GLC analysis. Chang and Miwa also explained the known fact that erucic acid has a high thermal stability against geometrical isomerization, on the basis of the reluctance of the excited singlet states to cross over to the triplet states. The extremely short-lived excited singlets need sensitization by stable triplets or by readily excitable free radicals like NO_2 and NO_2.

Wisniak (17) and Wisniak and Alfandary (18) were the first to report on the geometrical isomerization of jojoba oil with selenium and NO_2 catalysts under a wide range of conditions. Isomerization runs with selenium were conducted in a resin flask provided with heating and agitation. Overall time of reaction varied between 45 and 150 min, with 0.094–0.4% selenium, and temperatures 180–210 C.

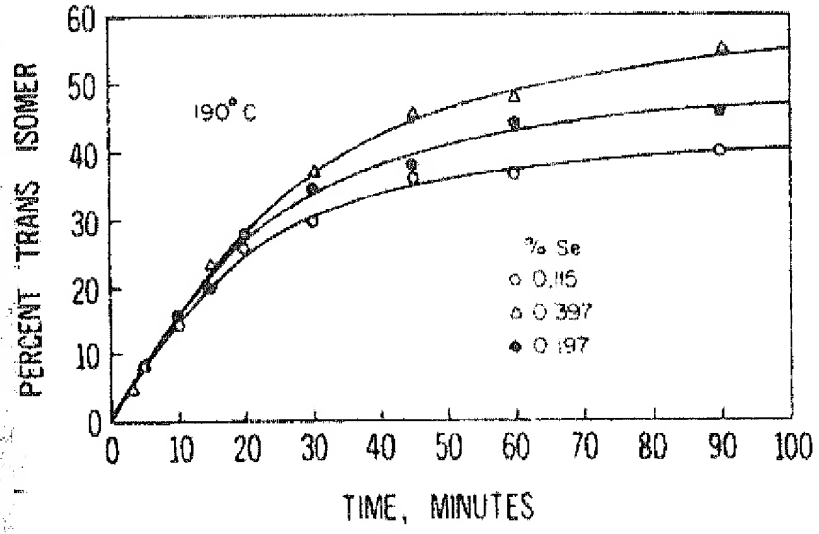


Fig. 2-4. Isomerization at 190 C with selenium (1%).

EXHIBIT 3

ester, 10%; and for the fatty acids and alcohols—octadecenoic acid, 6%; eicosenoic acid, 35%; docosenoic acid, 7%; eicosenoi, 22%; docosenol, 21%; and tetracosenol, 4%. On the basis of these results, Miwa (53) concluded that the liquid esters were not biosynthetized by random esterification of the fatty acids and alcohols. The GLC technique developed by Miwa has been improved by Duncan et al. (81) to decrease the time required by the HCl-hydrolysis step. They found that the wax is hydrolyzed faster by refluxing it in 5% HCl in anhydrous ethanol.

A more refined analysis using GLC coupled with high-pressure liquid chromatography, mass spectrometry and ozonolysis was

TABLE 1-26

Composition and Structure of Fatty Alcohols and Fatty Acids Derived from Jojoba Oil (Analysis by GLC, Ozonolysis-GC and GC-MS[a]

Alcohols	(%)	Acids	(%)
Tetradecanol	trace[b]	Dodecanoic	trace
Hexadecanol	0.1	Tetradecanoic	trace
Heptadec-8-enol	trace	Pentadecanoic	trace
Octadecanol	0.2	Hexadecanoic	1.2
Octadec-9-enol	0.7	Hexadec-7-enoic	0.1
Octadec-11-enol	0.4	Hexadec-9-enoic	0.2
Eicosanol	trace	Heptadecenoic	trace
Eicos-11-enol	43.8	Octadecanoic	0.1
Hecos-12-enol	trace	Octadec-9-enoic	10.1
Docosanol	1.0	Octadec-11-enoic	1.1
Docos-13-enol	44.9	Octadecadienoic	0.1
Tetracos-15-enol	8.9	Octadecatrienoic	trace
Hexacosenol	trace	Nonadecenoic	trace
		Eicosanoic	0.1
		Eicos-11-enoic	71.3
		Eicosadienoic	trace
		Docosanoic	0.2
		Docos-13-enoic	13.6
		Tricosenoic	trace
		Tetracosenoic	trace
		Tetracos-15-enoic	1.3

[a]Miwa (83, 84).

[b]Trace denotes 0.01–0.05%. Absence of absorption at 10.36 microns in infrared spectrophotometry indicates all ethylenic bonds to be *cis* in geometric configuration.

Mention of firm names or trade products does not imply endorsement or recommendation by the editors or contributors over other firms or similar products not mentioned.

Library of Congress Cataloging-in-Publication Data

Wisniak, Jaime.
The chemistry and technology of jojoba oil.

Bibliography: p.
Includes index.
1. Jojoba products. I. Title.
TP684.J64W57 1987 665'.35 87-22962
ISBN 0-935315-17-9

Printed in the United States of America

Exhibit 6

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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AFFIDAVIT
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Dear Assistant Commissioner:

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I, David Ashley, being duly sworn, depose and say as follows:

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Additionally, when fatty alcohols and fatty acids derived from jojoba oil are analyzed using infrared spectrophotometry, an absence of absorption at 10.36 microns indicates that all ethylenic bonds [of fatty alcohols and fatty acids derived from jojoba oil] are *cis* in geometric configuration. *See* Wisniak, at p. 43, *attached as* Exhibit 3. Therefore, fatty acids and fatty alcohols derived from jojoba oil are considered "trans-free".

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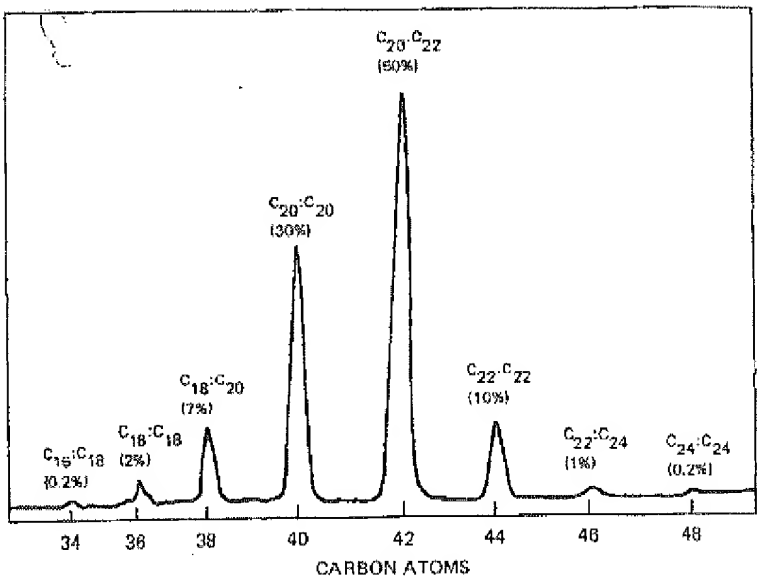
EXHIBIT 1



Jojoba oil esters are made up of fatty alcohols and fatty acids that are predominantly 20 or 22 carbon atoms long. Compared with most vegetable oils, the carbon chain lengths are remarkably uniform. (Information from T.K. Miwa)

alcohols are a mixture of eicosanol and docosanol, with smaller quantities of hexacosanol and alcohols of lower molecular weight.

The acids and alcohols that make up jojoba oil each have a single double bond. Moreover, all double bonds are in the ω_9 position (i.e., between carbon 9 and carbon 10, counting from the methyl end). This is a remarkable molecular purity, and the double bond position is different from that usually found in vegetable oils.

The nature of the oil can be grossly changed by reactions at the double bonds and ester functions, and many new products can result. One research laboratory in Israel, for example, has produced more than 40 different jojoba-based chemicals that appear to have commercial industrial applications.*

As in other natural oils, the double bonds in fresh jojoba oil are all in the *cis* configuration. However, they can be easily isomerized (twisted around in space), using as catalysts traces of selenium, nitrogen oxides, or active earth. This produces an equilibrium mixture with 20 percent *cis* and 80 percent *trans* double bonds. This simple process dramatically transforms the liquid into a soft, opaque cream resembling face cream. It can be stopped at various intermediate degrees of

* Information from A. Shani and J. Wisniak.

JOJOBA

New Crop for Arid Lands, New Raw Material for Industry

Report of an Ad Hoc Panel of the
Advisory Committee on Technology Innovation
Board on Science and Technology
for International Development
Office of International Affairs
National Research Council

NATIONAL ACADEMY PRESS
Washington, D.C. 1985

EXHIBIT 2

THE CHEMISTRY AND TECHNOLOGY OF

JOJOBA OIL

JAIME WISNIAK

American Oil Chemists' Society
Champaign, Illinois

percent nitrous acid. A 70% yield of *trans* isomer was obtained with no migration of the double bond. Their results indicated that the isomerization is induced initially by the nitrogen dioxide anion and followed immediately by complex formation between the excited triplet anion and the olefin. Crystallization of the final product yielded a solid that contained 96–97% of the *trans* form (brassidic acid) and melted at 58–59 C. The *cis* and *trans* double bonds in erucic and brassidic acids were identified by NMR, and absence of double bond migration was verified by reductive microozonolysis-GLC analysis. Chang and Miwa also explained the known fact that erucic acid has a high thermal stability against geometrical isomerization, on the basis of the reluctance of the excited singlet states to cross over to the triplet states. The extremely short-lived excited singlets need sensitization by stable triplets or by readily excitable free radicals like NO_2^- and NO_2.

Wisniak (17) and Wisniak and Alfandary (18) were the first to report on the geometrical isomerization of jojoba oil with selenium and NO_2 catalysts under a wide range of conditions. Isomerization runs with selenium were conducted in a resin flask provided with heating and agitation. Overall time of reaction varied between 45 and 150 min, with 0.094–0.4% selenium, and temperatures 180–210 C.

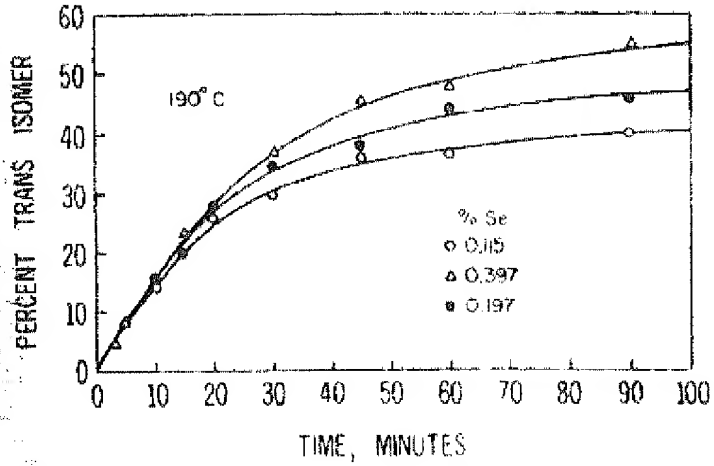


Fig. 2-4. Isomerization at 190 C with selenium (18)

EXHIBIT 3

ester, 10%; and for the fatty acids and alcohols—octadecenoic acid, 6%; eicosenoic acid, 35%; docosenoic acid, 7%; eicosenoi, 22%; docosenol, 21%; and tetracosenol, 4%. On the basis of these results, Miwa (53) concluded that the liquid esters were not biosynthetized by random esterification of the fatty acids and alcohols. The GLC technique developed by Miwa has been improved by Duncan et al. (81) to decrease the time required by the HCl-hydrolysis step. They found that the wax is hydrolyzed faster by refluxing it in 5% HCl in anhydrous ethanol.

A more refined analysis using GLC coupled with high-pressure liquid chromatography, mass spectrometry and ozonolysis was

TABLE 1-26

Composition and Structure of Fatty Alcohols and Fatty Acids Derived from Jojoba Oil (Analysis by GLC, Ozonolysis-GC and GC-MS[a]

Alcohols	(%)	Acids	(%)
Tetradecanol	trace[b]	Dodecanoic	trace
Hexadecanol	0.1	Tetradecanoic	trace
Heptadec-8-enol	trace	Pentadecanoic	trace
Octadecanol	0.2	Hexadecanoic	1.2
Octadec-9-enol	0.7	Hexadec-7-enoic	0.1
Octadec-11-enol	0.4	Hexadec-9-enoic	0.2
Eicosanol	trace	Heptadecenoic	trace
Eicos-11-enol	43.8	Octadecanoic	0.1
Hecos-12-enol	trace	Octadec-9-enoic	10.1
Docosanol	1.0	Octadec-11-enoic	1.1
Docos-13-enol	44.9	Octadecadienoic	0.1
Tetracos-15-enol	8.9	Octadecatrienoic	trace
Hexacosenol	trace	Nonadecenoic	trace
		Eicosanoic	0.1
		Eicos-11-enoic	71.3
		Eicosadienoic	trace
		Docosanoic	0.2
		Docos-13-enoic	13.6
		Tricosenoic	trace
		Tetracosenoic	trace
		Tetracos-15-enoic	1.3

[a]Miwa (83, 84).

[b]Trace denotes 0.01–0.05%. Absence of absorption at 10.36 microns in infrared spectrophotometry indicates all ethylenic bonds to be *cis* in geometric configuration.

Mention of firm names or trade products does not imply endorsement or recommendation by the editors or contributors over other firms or similar products not mentioned.

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Exhibit 7

FLORA.1100

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Kleiman *et al.*	Atty Docket No.:	FLORA.1100
Serial No.:	09/899,432	Group Art Unit:	1617
Filed:	07/06/2001	Examiner:	Shobha Kantamneni

TITLE: **ANTIVIRAL COMPOSITION AND TREATMENT METHOD**

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class mail in an envelope addressed to " Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" on:

Date: _____ By: _____

Printed Name: _____

AFFIDAVIT
PURSUANT TO 37 C.F.R. §1.132

Assistant Commissioner of Patents
Alexandria, VA 22313-1450

Dear Assistant Commissioner:

STATE OF ARIZONA)

:

COUNTY OF MARICOPA)

I, David Ashley, being duly sworn, depose and say as follows:

I received a Bachelors of Science in Chemistry from Arizona State University in May of 1987. I have been employed by International Flora Technologies, Inc., (Technical Department) since 2003 where I serve as a chemist. Previously, I was employed at Safety-Kleen Systems, Inc., where I served as Compliance Manager from 2002-2003. I have also worked in various technical and managerial capacities at Onyx Environmental Services (Salesco Systems USA, Inc.), ADFlex Solutions Inc., and Revlon Consumer Products Corporation. I have over fourteen years of experience in analytical chemistry, environmental, health, and safety management. I am a Certified Hazardous Material Manager, and a member of the American Chemical Society.

I have undertaken an extensive review of United States Patent Application Serial No. 09/899,432 in conjunction with the Sintov *et al.* reference (WO 9602244 A1). The Sintov *et al.* reference is directed toward topical pharmaceutical compositions that include salts of fatty acids, specifically: linoleates, elaidates, palitates, myristates, oleates, malonates, succinates, adipates, pimelates, maleates, fumarates and azelates.

The invention referenced in Application Serial No. 09/899,432 is directed to methods for treating virus-induced and inflammatory diseases utilizing topical compositions that include monounsaturated long chain alcohols in combination with long chain fatty acid salts and fatty acid esters. More specifically, the salts of long chain fatty acids include fatty acids with chain lengths of 20 carbons or greater.

Salts of fatty acids are obtained through saponification of the fatty acids. It is general knowledge that solubility of fatty acid salts decreases with an increase in chain length of the fatty acids, and therefore chain length of fatty acids are a consideration in the manufacture of topical applications. *See* Exhibit 1, *excerpt from* Baileys Industrial Oil and Fat Products, 6th ed., vol. 6, page 106 (2005). The table in Exhibit 1 illustrates common fats and oils used in saponification of commercial products, and all of these fats and oils comprise carbon chain lengths of 18 carbons or less. Carbons with longer chain lengths than those illustrated in the table (*e.g.*, longer than C18) are "generally insoluble at room temperature".

The Sintov *et al.* reference follows this general knowledge in identifying "preferred" salts for "use in the present invention is a water-solubilized C_{16}-C_{18} carboxylic acid salt." *See* Sintov *et al.*, page 3, lines 1-2.

By contrast, the invention referenced in Application Serial No. 09/899,432 utilizes salts of fatty acids with carbon chain lengths of 20 carbons or greater in combination with monounsaturated alcohols and mixed esters for topical applications for treatment of viral infections and inflammatory diseases. The effect of the combination referenced in this invention is a dramatic increase in antiviral activity. This effect could not have been expected based on the general knowledge available because salts of fatty acids with carbon chain lengths of 20 carbons or greater would generally have been thought to hinder absorption due to their insolubility. In other words, a 100-fold increase in

antiviral activity is observed where the expectation would be that the delivery mechanism would not traffic the antiviral as effectively due to the decreased solubility associated with fatty acid salts having chain lengths of 20 carbons or greater.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true. I further declare that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful and false statements may jeopardize the validity of the subject patent application or any patent issued thereon.

I further declare that I have received no special compensation or consideration for making this affidavit, nor have I been in any way told, either directly or by implication or inference, by anyone that my employment by International Flora Technologies, Inc., or my professional advancement or other matters of personal or professional interest to me depend in any way on whether or not I make this affidavit or the content thereof. I further declare that I make this affidavit of my own free will and choice without any duress or influence of any kind, believing fully in the truth of the statements made by myself herein.

David Ashley

I, Carol Hynes, a Notary Public in and for the County and State aforesaid, do hereby certify that David Ashley, whose name is subscribed to the foregoing instrument, appeared before me this day in person and acknowledge that he signed, sealed and delivered the said instrument as his free and voluntary act and deed for the uses and purposes therein set forth.

Given under my hand and Notary Seal this 25th day of March 2008.

My commission expires on Nov. 29, 2011

SEAL

CAROL HYNES
Notary Public - Arizona
Maricopa County
My Comm. Expires Nov 29, 2011

BAILEY'S INDUSTRIAL OIL AND FAT PRODUCTS

Sixth Edition

Volume 6

Industrial and Nonedible Products from Oils and Fats

Edited by

Fereidoon Shahidi

Memorial University of Newfoundland

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WILEY-INTERSCIENCE

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TABLE 1. Fatty Acid Compositions of Common Fats and Oils.[a]

Common Name	Chemical Name	Chemical Formula	Symbol	Animal Fats, %		Vegetable Oils, %		
				Tallow	Lard	Coconut	Palm kernel	Soybean
			Saturated Fatty Acids					
caprylic	octanoic	$C_8H_{16}O_2$	C 8			7	3	
capric	decanoic	$C_{10}H_{20}O_2$	C10			6	3	
lauric	dodecanoic	$C_{12}H_{24}O_2$	C12			50	50	0.5
myristic	tetradecanoic	$C_{14}H_{28}O_2$	C14	3	1.5	18	16	0.5
palmitic	hexadecanoic	$C_{16}H_{32}O_2$	C16	24	27	8.5	8	12
margaric	heptadecanoic	$C_{17}H_{34}O_2$	C17	1.5	0.5			
stearic	octadecanoic	$C_{18}H_{36}O_2$	C18	20	13.5	3	2	4
			Unsaturated Fatty Acids					
myristoleic	tetradecenoic	$C_{14}H_{26}O_2$	C14:1	1				
palmitoleic	hexadecenoic	$C_{16}H_{30}O_2$	C16:1	2.5	3			
oleic	octadecenoic	$C_{18}H_{34}O_2$	C18:1	43	43.5	6	14	25
linoleic	octadecadienic	$C_{18}H_{32}O_2$	C18:2	4	10.5	1	2	52
linolenic	octadecatrienic	$C_{18}H_{30}O_2$	C18:3	0.5	0.5	0.5		6

[a]From historical data and Procter & Gamble analyses.

are practical considerations that must be addressed when performing this reaction on a commercial scale.

Compositional differences in the fats and oils give rise to their significantly different physical properties and those of the resulting fatty acids and soaps. Fats and oils are triglycerides composed of glycerol ester linked to three fatty acids. The main compositional difference is the chain-length distribution of the fatty acids associated with the fats or oils. The compositions found in some commercially important fats and oils are summarized in Table 1. High levels of unsaturated (containing double bonds) or short-chain-length components produce fatty acids that are liquid and soaps that have high water solubilities at room temperature. Conversely, high levels of saturated, long-chain-length components produce waxy and hard fatty acids, e.g., candle wax, and soaps that are essentially insoluble at room temperature. Furthermore, unsaturated components are more susceptible to oxidative degradation, i.e., the oxidation of the double bond to form a number of shorter chain components. This gives rise to undesirable odors and darker colors. A key to producing soaps with acceptable qualities is the proper blending of these fats and oils.

The quality, i.e., level of impurities, of the fats and oils used in the manufacture of soap is important in the production of commercial products. Fats and oils are isolated from various animal and vegetable sources and contain different intrinsic impurities. These impurities may include hydrolysis products of the triglyceride, e.g., fatty acid and mono/diglycerides; proteinaceous materials and particulate dirt, e.g., bone meal; and various vitamins, pigments, phosphatides, and sterols.